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1. ABOUT GENOVESA

GENOVESA is a sophisticated web-based platform that offers a comprehensive suite of tools for analyzing genomic data, generating reports, and providing internal clinical interpretation. With its user-friendly interface and powerful features, GENOVESA enables researchers and clinicians to easily explore and interpret sequencing data, identify clinically relevant variants, and generate informative reports. From variant calling and annotation to filtering and classification, GENOVESA is empowering users to make informed clinical decisions with ease.

2. SOFTWARE REQUIREMENTS

For optimal performance with the GENOVESA software, we recommend a minimum internet connection speed of 10 Mb/s and a full HD screen. These requirements will help ensure the best possible user experience while using our software.

3. REGISTRATION

To register for a product on the GENOVESA homepage, please follow these steps:

- Go to <https://ngs-GENOVESA.biovendor.group/>.
- Select the desired product line.
- Click on the "Register" button and fill in your information in the form provided.
- Ensure that all fields marked with an asterisk (*) are completed, as they are mandatory.
- After you submit the registration form, a member of our sales team will follow up with you via email.

4. FIRST SIGN IN

Once you have received your credentials, please follow these steps to sign into your account on the GENOVESA homepage:

- Go to <https://ngs-GENOVESA.biovendor.group/>.
- Click on the "User" icon located in the top right corner of the page and select Sign in.
- Enter your credentials to sign in.

If this is your first time signing in, please ensure that your account is connected to your organization (subject). To check if your account is connected, your name and joined subject will be displayed in the top right corner of the page. If your organization's name is not visible, you will need to select the subject by following the instructions in the "Changing subject" section of this user guide. Once you have joined a subject, you will be able to view projects connected to your organization.

5. PASSWORD CHANGE

To change your password, please follow these steps:

- Navigate to the top right corner of the page and select the "User" icon .
- In the dialogue window that appears, input your new password.
- Click "OK" to save your new password.

6. CHANGING SUBJECT

Your GENOVESA account may have access to multiple subjects; however, it can only be assigned to one subject at a time. If you need to switch between subjects, please follow these steps:

- Navigate to the top right corner of the page and select "User" icon .
- Click on "Join to existing profile".
- You will be redirected to a table containing all subjects that are available for your account.
- Select the subject you want to switch to by clicking on it.

Once you have switched to the new subject, you will be able to view and manage the projects associated with it.

7. NAVIGATING THE APPLICATION

Upon logging in, you will be directed to the GENOVESA homepage. Depending on the product with which you registered, you will either see a PRO or FASTGEN tab in the top panel.



1. In the PRO tab, you can find projects related to ViennaLab NGS Assay kits.
2. In the FASTGEN tab, you can find projects related to BioVendor fastGEN kits.
3. Your name and current subject are displayed on the top right side of the page.
4. You can change your password, change your current subject, or sign out by clicking on the "User" icon .

When you click on PRO or FASTGEN tab, you will be directed to a Projects table that displays all projects created in your current subject.

Clicking on a row in the Projects table will display all associated samples in the table below.

Projects

ADD PROJECT 

ID	Project Name	Workflow	Status	Created	Finished
809	FastGen Solid - demo	FastGen SOLID (KRAS, NRAS, BRAF)	PASSED	10. 09. 2022	14. 09. 2022

Clicking on a row in the Samples table will display all variants associated with the selected sample.

Samples of project FastGen Solid - demo

ID	<input type="checkbox"/>	SampleID	Status	Total reads	Total Variants
8920	<input type="checkbox"/>	<input checked="" type="checkbox"/> BV-Solid-1-PC	PASSED	71 032	5
8921	<input type="checkbox"/>	<input checked="" type="checkbox"/> BV-Solid-2	PASSED	105 822	1

8. CREATING A PROJECT

The first step in your data analysis is to set up a project. Please follow these steps to create a new project:

1. Click on "ADD PROJECT" and fill in the fields as shown below:
 - Project Name: Provide a descriptive name for your project. This text is for your information only and can be edited retrospectively. It does not impact the analysis.
 - Workflow: Select the desired analysis. This field is mandatory and cannot be changed after submission.
 - Sequencer Technology: Select the sequencer that was used for your project. GENOVESA will expect the number of FASTQ files based on the selected sequencer. This field is also mandatory and cannot be changed after submission.
 - Description: You may provide more detailed information about your project in this field. This text is for your information only and can be edited retrospectively. It does not impact the analysis.
2. Click on "Submit". Your new project will be displayed in the Projects table with a status "NEW".

9. EDITING PROJECT NAME OR DESCRIPTION

To modify the Project Name or Description displayed in the Projects table, follow these steps:

1. Navigate to the Projects table.
2. Click on the blue "Edit project, upload / download data" icon corresponding to the project you want to edit.

Workflow ↕	Status	CNV	Created	Finished	Description ↕	Edit project, upload / download data		
FastGen SOLID (KRAS, NRAS, BRAF)	PASSED		10. 09. 20 22	14. 09. 20 22	Biovendor demo run for FastGen Solid cancer kit			

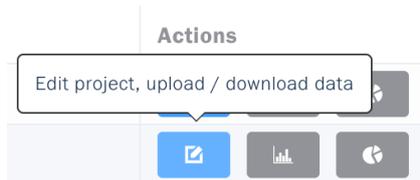
3. In the tab that opens, you can modify the Name or Description fields.
4. Once you have made the desired changes, click on the "UPDATE" button to save them.

Your Project Name or Description will now be updated and displayed in the Projects table.

10. UPLOADING FASTQ FILES

Before starting your analysis, you must first upload your FASTQ files. To do this, please follow these steps:

1. Navigate to your Projects table and click on the "Edit project, upload / download data" button.



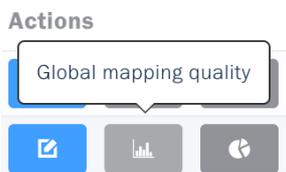
2. Select the "FASTQ Files" tab and click on "SELECT FILES".
3. In the dialogue window with the file browser, select the files that you wish to upload.
4. Click "START UPLOAD" and wait for the upload to be completed. Do not close the window during the upload process. You can open another tab or window with GENOVESA to check on the progress of the analysis or even view the results.

GENOVESA will automatically initiate the analysis once any FASTQ file for a sample is uploaded. The status of your project will change from "NEW" to "ANALYSING". Once the analysis is complete for all uploaded samples, the Project status will change to "PASSED".

! Please note that only raw FASTQ files should be uploaded for analysis. Do not alter the FASTQ files in any way, including renaming the files or trimming the reads. This is important to ensure accurate and reliable analysis results.

11. VIEWING DATA QC

Once your analysis is complete, you can access several quality control (QC) metrics. For the entire project, you can view Global Mapping Quality and FASTQC. To view the Global Mapping Quality, click on the "Graph" icon located in the Actions column of the Projects table. Excel sheet will be downloaded automatically.



To view the FASTQC, click on the "Pie chart" icon located in the same column.



To view the QC metrics for an individual sample, select the project and scroll down to the Samples table. Then, select the corresponding "Graph" or "Pie chart" icons from the Actions column.

12. VIEWING VARIANTS

Once a sample has reached the status PASSED, you can view its results in the Variants table. To access the Variants table, click on a row in the Samples table and scroll down. From there, you can view the called variants, filter, and sort them by various parameters, and export the table for further analysis.

There are multiple tabs available:

Variants

ViennaLab Filter	All Variants	Custom Filter	Preselected Variants	Signed Out Variants
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1. The ViennaLab Filter tab displays only variants that have passed a predetermined set of filtering rules established by GENOVESA. These rules are specific to each assay kit.
2. The All Variants tab presents all called variants found in the sample's VCF file, without any additional filtering applied.
3. The Custom Filter tab enables users to apply their own filtering parameters to all variants found in the sample.
4. Preselected Variants tab shows only variants that have already been preselected or signed out.
5. Signed Out Variants tab shows only variants that have been signed out.

The Variants table displays rows of identified variants along with their core annotations, which are presented in columns:

- *Sample ID* - Sample name in which the variant was found.
- *Int. Cl. A, Int. Cl. B* - Internal classification of the variant. To change the classification, click on the number. GENOVESA will show this classification for this variant across all Projects in the current subject.
- *ACMG* - ACMG prediction is established by a defined set of rules. To view the rules applied to a specific variant, click on the corresponding number.
- *Freq / Proj* - Displays frequency of the variant in the current project.
- *Freq / Som (Germ)* - Displays frequency of the variant in the same workflow type in your subject.
- and more standard variant annotation (Gene / Transcript, Chr:Position, HGVS_c/HGVS_p, Type, Consequence, Var Quality, VAF, Total Depth, Genotype)
- and multiple databases: dbSNP, gnomAD MAX AF, Impact, COSMIC.

ClinVar and ACMG values:

- 0 - None / not provided
- 1 - Benign
- 2 - Likely benign
- 3 - Uncertain significance
- 4 - Likely pathogenic
- 5 - Pathogenic

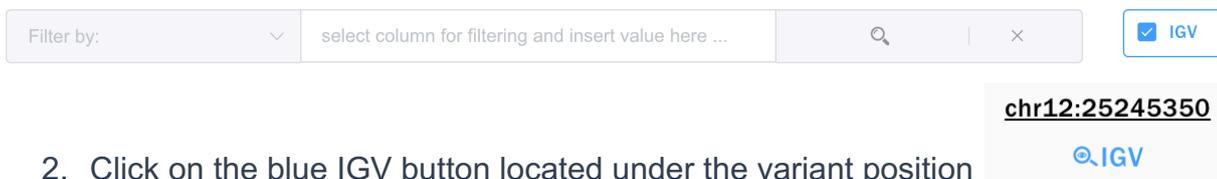
The Internal Classification feature enables users to classify variants according to their own criteria. This classification is applied across all projects and can be used for filtering purposes. In addition to the standard 0–5 classification system, users may assign more descriptive classes to the variants:

- CI - Conflicting interpretation
- PS - Pseudogenes
- RF - Risk Factor
- DA - Disease Association
- DR - Drug Response
- PR - Protective
- PA - Phenotype Association
- PM - Polymorphic
- IV - Intronic Variants
- SA - Sequencing Artifact

13. VIEWING A VARIANT IN IGV

To view specific variant in the browser version of IGV:

1. Tick IGV checkbox next to the Filtering field on the top of the Variants table



2. Click on the blue IGV button located under the variant position
3. Scroll down under the Variants table.

The position of the variant will be centered in the IGV viewer.

The browser IGV loads only parts of the sample BAM file for optimal performance. However, if you need to navigate to a specific position, you can do so by entering the coordinates in the top left corner of the IGV browser. This will load the desired location in the browser, allowing you to view the corresponding reads and variants at that location.

14. PRESELECTING AND SIGNING OUT VARIANTS

To select variants for a report, you need to first sign them out. This indicates that you have reviewed and validated variants for the sample. Preselected variants can be used for temporary preselection if you want to return to the sample variants later. However, the report will only include variants that have been signed out.

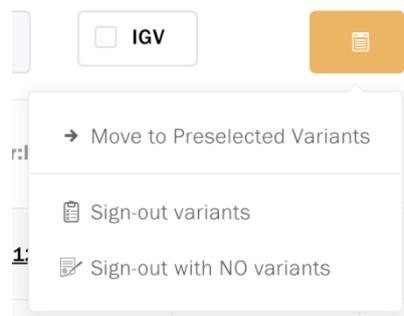
To preselect or sign out a variant:

1. Tick checkbox in the first column in the Variants table for desired variants.

Transcript system: Ensembl RefSeq Filter by:

	<input type="checkbox"/>	Sample ID	Int. Cl. A	Int. Cl. B	ACMG	ClinVar
>	<input checked="" type="checkbox"/>	BV-Solid-1-PC	0	0	4	5
>	<input checked="" type="checkbox"/>	BV-Solid-1-PC	0	0	3	5
>	<input type="checkbox"/>	BV-Solid-1-PC	0	0	4	3

2. Click on the orange "File" icon and select one of the options shown below:



The preselected and signed out variants can now be seen in the corresponding tabs.

To remove signed out variants from the Signed Out Variants table to Preselected table:

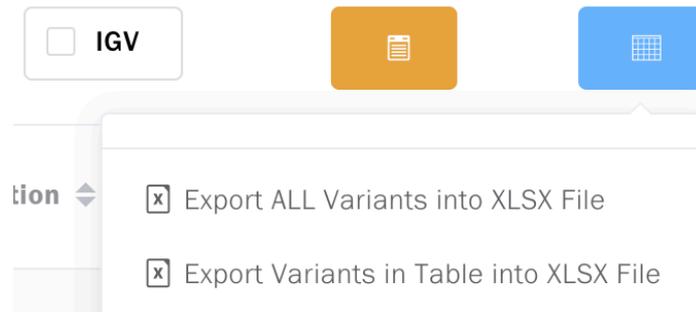
1. Navigate to the Signed Out Variants tab.
2. Click on the orange "File" icon and click on Sign-out RESET.
3. This will move all your signed out variants to the Preselected table.

To remove variant/s from Preselected table:

1. Navigate to the Signed Out Variants tab and sign-out reset all variants.
2. Navigate to the Preselected Variants tab.
3. Tick a box in the first column to select which variant/s should be removed.
4. Click on the orange "File" icon and click on Remove from Preselected Variants.

15. EXPORTING VARIANTS TO XLSX

To export variants in the current Variants table or All variants for the selected samples, click on the blue "Table" icon on the top right of the table and select one of the options in the drop-down menu. The file will be downloaded to your computer, and you can open it in a spreadsheet editor for further analysis or manipulation.



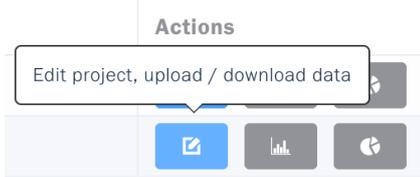
16. CREATING A REPORT

To create a report for a single sample, please follow these steps:

1. Navigate to the Samples table and locate the sample for which you want to create a report.
2. Click on the blue "Manage data of examination" button  for the chosen sample.
3. Fill in all the required fields in both tabs of the pop-up window that appears.
4. Click "Save" to save the information.
5. Go to the Variants table and locate any variants that you want to include in the report.
6. Sign out any desired variants by selecting them and clicking the orange "File" icon , then selecting "Sign out variants".
7. If there are no variants to sign out, click on the orange "File" icon  and select "Sign out with NO variants."
8. Click on the orange "File" icon again and select "Make Report - PDF file."
9. The report will begin downloading in PDF format.

17. DOWNLOADING DATA

Downloading result files of the analysis can be done by selecting the "Edit project, upload / download data" button in your Projects table.



Tabs currently available and their content:

- FASTQ – FASTQ files that have been uploaded by the user.
- Result Files – VCF files for each sample.
- MultiQC & Metadata Files – FASTQC zip and html files for each sample, HS metrics.
- Other Files – Files specific to each kit e.g., trimming and coverage GAPs stats or TMB files.
- BAM / BAI Files - BAM and BAI files for each sample.

Thank you for your interest in our products. If you have any questions or require further assistance, please do not hesitate to contact us via email provided on the bottom of the web page.